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M. D. T H E S I S .

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THE DIAGNOSIS AND TREATMENT OF DIPHTHERIA.

Sent by:-

Henry Edwards, M.B.C.M., 1890.
Trefeddyg,
PORT DINORWIC,
NORTH WALES.





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THE DIAGNOSIS AND TREATMENT OF DIPHTHERIA.

Diphtheria is an acute infectious disease due to the presence and activity of the Klebs-Loeffler bacillus, and characterized by the production of false membrane on a mucous, or abraded skin surface.

It is primarily a local disease, but becomes general owing to the production of toxins.

The disease generally commences in the fauces, but sometimes in the larynx, nose, or other mucous surface, or less frequently on an abraded skin surface.

Diphtheria may be classified as:-

- (1). Pure or simple, when caused by the Klebs-Loeffler bacillus alone.
- (2). Mixed, Impure, or Complex, when due to other organisms besides the specific bacillus.

It may also be classified according to its site: e.g. Diphtheria of the Throat or Angina; Diphtheria of the Larynx or Croup; Nasal Diphtheria; Diphtheria of the trachea or bronchi &c.

Diphtheria of the Throat or Angina is by far the commonest form, the membrane being formed here in about 90 % of cases. Of 1,000 cases reported by Lennox Browne, 84 % were

situated above the larynx; 672 affected the fauces alone; and 165 affected the fauces and nose.

The incubation period is from 12 hours to 4 days, probably never exceeding 7 days.

Clinical Diagnosis:- The onset of the disease is either sudden or gradual. As a rule it begins suddenly in young children, and may begin suddenly in older patients also.

But one often finds adults who have had the disease for days without feeling much inconvenience from it. Again, patients are seen who are troubled by the sequelae only, and have not felt ill from the disease itself.

The prodromal symptoms are a sense of lassitude, pain in the back or all through the body, headache, with some rise of temperature, simulating influenza, for which it may be mistaken, unless the throat be examined.

These are, as a rule, followed by the early throat symptoms; but sometimes, though rarely, the throat symptoms may be delayed for a few days.

There may be pain in the neck, and some pain at the angle of the jaw; but the pain in the throat is not sufficient to cause difficulty in opening the mouth or on swallowing.

In a short time the local throat symptoms become manifest. There is a feeling of dryness in the throat with a desire to hawk and clear it.

The voice becomes hoarse; and there is often some hoarse cough especially in children, even before there is membrane formed in the larynx. The breathing is often stridulous. The throat at the earliest stages presents a general redness, which is more marked at the seat of the future membrane. The fauces are red and swollen. The tonsils and fauces soon show patches of exudation. One of the tonsils is the most frequent starting point of the exudation. In Lennox Browne's 1,000 cases the tonsil was the primary seat of lesion in all the faucial cases. According to Northrup however the posterior pillars are often so also, but the anterior pillars rarely so.

At first the membrane appears as a thin, whitish, or opalescent pellicle, resembling the fresh mark of lunar caustic; or, in lacunar diphtheria, it may begin in small, whitish specks, which coalesce. This pellicle can be detached. But the membrane soon becomes thicker, more adherent, and of a greyish white colour.

As the disease advances, it becomes yellowish grey, brownish, and black.

When one tonsil is first attacked, the other one is often soon affected.

The membrane tends to spread backwards and forwards, to the larynx, anterior pillars

of the fauces, uvula- especially ^tis posterior surface, mouth, soft and hard palate, nose, Eustachian tubes, gums &c.

The membrane is not deposited at the same time in all the parts affected. So there is a difference in its colour and consistency at different parts, the more recent membrane being of a lighter colour and of less thickness than that first formed. The membrane is usually tough, thick, and adherent to the under-lying surface, and, on detachment, leaves a raw bleeding surface. But it may be thin, friable, and easily detached. Sometimes a thin reticulum is seen at its edges; but, at other times, the edges are thicker than the centre, and become everted when the membrane is about to separate.

The membrane of pure ^hdiphtheria, is, as a rule, lighter in colour than that of the complex form, and is attended with less swelling of the submucosa. Microscopically, the membrane shows a dense homogeneous layer of fibrin, with the surface of the epithelium more or less swollen and disintegrated beneath. A few epithelial cells may remain at some parts; but the epithelium soon disappears. As a rule the membrane is separated from the epithelium by a space containing granular material and leucocytes.

The superficial layer is filled with the specific bacilli and with buccal microbes.

The specific bacillus may be seen in the deeper parts, but is found more abundantly on the superficial layers. The streptococcus and staphylococcus may also be present in the superficial and deeper layers, and pass much deeper into the tissues than the specific bacillus.

The exudate is also found in the lower strata and around the lymphatics and blood vessels, which it constricts.

Thus the membrane becomes adherent to the underlying tissues. As the disease advances, the constriction of the blood vessels causes ulceration and gangrene of the lower part and separation of the membrane.

Bacteriological Diagnosis:- The bacteriological diagnosis of ^diphtheria depends upon the discovery of the specific bacillus.

If possible, a portion of the membrane is removed with forceps or wire covered with absorbent non-antiseptic cotton wool. If this is not possible the surface of the membrane may be scraped with a platinum loop. Or, if no membrane be within reach, the surface of the pharynx may be swabbed with cotton wool. The membrane or swab is then placed in a sterile test-tube.

The membrane or swab, held by forceps, is then rubbed over the surface of a clean cover-glass. The film is then dried and fixed to the cover-glass by passing it quickly through the flame. It is then stained by a saturated solution of methylene blue or Loeffler's solution.

After staining 2 or 3 minutes the film is washed in water, dried, and mounted for microscopical examination. In some cases the bacilli are so numerous and characteristic as to leave no doubt of the diagnosis. But often, if found, they are by no means as typical as those seen in culture.

The bacilli are motionless slender rods, straight or slightly curved, usually 3μ in length, varying from 1μ to 6μ .

Their diameter varies from $.3\mu$ to $.8\mu$. According to Schabad the ratio of the length to the diameter varies from 5 : 1. to 8 : 1.

They are not uniformly cylindrical, a bulging being often seen at the ends. They may be also wedge-shaped, or be pointed at both ends and swollen in the middle. Their chief characteristic is polymorphism. Sometimes club-shaped, and spindle-shaped bacilli are seen.

They stain deeply with the blue, sometimes being uniformly coloured, but often showing in their substance little granules more darkly

stained, so that a dotted or beaded appearance is presented. Sometimes the ends are swollen and more darkly stained than the rest, giving a club-shaped appearance, distinct clubbing being less frequently seen than in cultures.

In some specimens these swellings and granules stain of a violet tint. Another reputed characteristic appearance is occasionally seen, as if the protoplasm were shrinking from the cell wall, leaving ^a more or less regularly uncoloured or lightly coloured space at the periphery.

The bacilli lie irregularly scattered, singly, in pairs, or in clusters having a tangled appearance. Sometimes they lie parallel to each other, or form an acute or obtuse angle with each other, or have a close resemblance to letters of the alphabet - v, x, m, n, &c.

If several bacilli form a chain it is usually a broken one and not a straight line.

If the presence of mouth microbes confuse the eye, this can be obviated by Gram's method of staining, which leaves the buccal microbes invisible.

If no specific bacilli are found by the above process, it may be repeated. If they are found nothing further is necessary, unless it be desired to confirm the diagnosis.

If no bacilli have been found, or if we desire confirmatory evidence, we may go ^{on} to the culture method. Bacilli grow best ^{at} 36° C or 37° C.

According to Muir and Ritchie growth ceases at 20° C. According to Park it may occur at 41° C. Solidified blood serum is the best medium for the growth of the bacillus, and is the one most generally used for diagnosis. The culture may be by swab or needle. That by a swab is as follows: a sterile swab is well rubbed on the mucous membrane of the pharynx and tonsils, and especially on any ~~diphtheritic~~ membrane present -- the oldest

membrane being chosen. The culture medium is then rubbed thoroughly with the swab without breaking the surface of the serum. This should be done without contaminating the swab. The culture tube is then plugged. The needle or streak culture method is as follows:- A piece of exudation or membrane is removed by means of a platinum needle, with which two or three parallel lines are drawn close together over the surface of the culture medium, firmly but without disturbing the surface.

The culture tube is then plugged. After 12 to 24 hours growth the colonies appear as small circular discs of opaque whitish colour, their centre being thicker and of a darker greyish appearance than the periphery when viewed by trans-

mitted light. They attain a diameter of $1\frac{1}{2}\mu$ to $2\frac{1}{2}\mu$ in 24 hours. On the second or third day, they may be 4μ , but when numerous they remain smaller. The colonies do not liquefy the serum.

According to Roux, if the colonies do not appear in 24 hours a negative diagnosis may be formed as regards ~~that~~ particular culture.

After 24 hours colonies of other microbes appear, e.g., the streptococcus, which do not appear until after 24 hours, and whose colonies are much smaller than those of the diphtheria bacillus, and have a whitish appearance.

Those of the staphylococcus take 2 or 3 days to grow properly. They are much bigger than those of the bacillus diphtheriae. . On the agar media the specific colonies have much the same appearance as on blood serum, but grow more slowly and sometimes may be comparatively smaller.

In bouillon with a little glucose they grow well. The bouillon becomes acid in 2 or 3 days, and several days later becomes alkaline.

In 4 or 5 days a turbidity appears in the bouillon, which soon settles to the bottom, and forms a powdery layer at the sides of the vessel.

In 2 or 3 weeks the cloudiness begins to clear, and in several months the bouillon becomes quite clear.

The colonies are examined microscopically. This is done by passing a sterile platinum loop through several of the colonies and washing this in a drop of water placed on a clean cover-glass, which is then dried in the air and passed through the flame to fix. It is then stained for 10 minutes with a methylene blue solution, washed, dried, and mounted in balsam.

The bacilli show the same character as in the membrane, but the irregularity in the staining is more marked. A culture examined from day to day shows marked changes in the shape and size of the bacilli.

The diagnosis may be further confirmed by making sub cultures and testing these by the inoculation of animals. The local and general changes are then watched. Loeffler states that in rabbits and guinea-pigs the bacilli produce no change on healthy mucous membranes, but when the latter are injured by scarification or otherwise the production of false membrane results.

This membrane is usually less firm than in human diphtheria, and the bacilli in it less numerous. Sub-cutaneous injection in guinea-pigs of a sufficient dose of bacilli produces death in 36 hours. (Muir and Ritchie).

If a 3 or 4 weeks broth culture be filtered,

and the filtrate be injected into guinea-pigs, there is a local inflammatory oedema but no membrane. If the animals live long enough paralytic phenomena may occur, the hind limbs being usually affected first, the paralysis then extending to other parts, though sometimes the fore limbs and neck are first affected.

Sometimes symptoms of paralysis do not appear until 2 or 3 weeks after inoculation.

After paralysis has appeared a fatal result usually follows in the smaller animals; but in dogs, recovery may take place.

Rats and mice possess a high degree of resistance to the toxin. Roux and Yersin found that 2 c.c. of toxin, which was sufficient to kill a rabbit in 60 hours, had no effect on a mouse; whilst of this toxin even $\frac{1}{15}$ c.c. produced extensive necrosis of the skin of the guinea-pig.

Diphtheria bacilli differ greatly in their degree of virulence. Some are rapidly fatal for guinea-pigs and extremely virulent.

Many writers -- notably Brieger, Frankel, and Wright have described absolutely avirulent and atoxic *diphtheria* bacilli. Roux and Yersin failed to restore the virulence of those bacilli which had lost it completely; but Bomstein succeeded in doing so by introducing into the bodies of animals cultures of virulent bacilli

in celloidin sacs and repeating the operation a number of times. The occurrence of the avirulent bacilli has given rise to a controversy concerning the so-called pseudo-diph^htheria bacilli.

The avirulent diph^htheria bacilli are in all respects identical with true diph^htheria bacilli save in the presence of virulence and power of producing toxins; but, according to some observers, the pseudo-diph^htheria bacilli differ in ~~all~~ other respects also. Roux, Yersin, Behring, and others believe in the identity of the two organisms; but, by far the larger number of observers believe that there is always a difference between the two, and that under no known conditions of growth can the one class change into the other.

Schabad mentions the following points of difference:-

1. Growth on Agar. Pure cultures of the two classes grow well. The colonies of the pseudo-bacilli are usually of a yellow colour, more luxuriant and fluid than true bacilli; the colour of the latter is usually grey.

The differences between the two are more pronounced after 2 or 3 days growth.

2. In ascitic fluid the pseudo-bacillus gives a distinct cloudiness whilst the true does not.

3. Morphology. To judge by this the two organisms must be placed as nearly as possible under the same conditions of growth. Thus the pseudo-bacillus has a ratio of length to breadth of 2 : 1 to 4 : 1; whilst that of the true bacillus is from 5 : 1 to 8 : 1. The pseudo-bacillus stains more regularly also.

4. With Neisser's stain a 9 to 24 hours culture shows, in the true bacillus, the body stained a brownish yellow, while at one or both ends may be seen the so-called polar granules as deeply-coloured blue oval shaped areas, the diameter of which is greater than that of the bacillus in which they are seen. These granules are only seen in old cultures in the pseudo-bacillus.

5. Reaction in bouillon cultures. Grown in broth, neither too acid nor too alkaline, to which a trace of glucose has been added, the true bacilli form acid in a day or two, whilst the pseudo-bacilli either form alkali from the beginning, or a very small amount of acid which is soon neutralized and goes over to alkali.

6. Pathogenesis to animals. The pseudo-bacilli are non-pathogenic. The true bacilli, except the avirulent forms, are pathogenic. Both the true and false bacilli cause local oedema when injected into guinea-pigs; but no oedema occurs in the case of the true bacilli when a

suitable dose of anti-toxic serum is given from 6 to 16 hours before inoculation; whereas it has no effect in the case of the pseudo-bacilli.

According to Muir and Ritchie a positive result on inoculating a guinea-pig with 1 c.c. of a 24 hours broth culture is conclusive evidence; and, for all practical purposes, an organism having all the microscopical and cultural characters of the ^d~~d~~iphtheria bacillus may be accepted as such.

General Symptoms. The tongue in ^d~~d~~iphtheria is not characteristic. It may be fairly clean before the membrane has formed; but may be ~~extreme~~ foul, especially in septic cases.

The breath as a rule is foul if the disease is advanced and fairly severe.

Fever is generally moderate, rising gradually to 103° , unless there be complications when it may rise to 106° or so. In an uncomplicated case it is usually about 101° about the third day.

When the membrane is fully formed there is a gradual fall. A further rise shows an ~~ext~~ension of the membrane or the occurrence of some complication. The temperature is generally low in comparison with the acuteness of the constitutional symptoms, and is always irregular.

It is not characterisitic, and does not afford reliable indications of the severity of the disease

Still a gradual fall is a favorable sign, but a sudden fall to or below normal is usually a bad sign, as it is due to asthenia.

In complex dip^htheria the temperature^{is more apt} to be higher and remittent than in pure diptheria.

The Pulse as a rule at the beginning of the disease is very rapid, especially in proportion to the temperature, as it is governed by the amount of toxaemia. It is often of low tension, and may be irregular as regards rhythm and tension.

Sometimes there is bradycardia, which is of bad omen. A very quick pulse is also a grave symptom, especially if over 150 a minute.

Adenitis is present in most cases. If the case be mild the inflammation may not be evident; but if severe it is quite evident.

In pure diptheria the cervical glands are most often affected. They are a little tender and swollen and can be distinctly felt, as the surrounding tissues are not affected.

In severe cases, they are much swollen, as the swelling varies with the extent and intensity of the disease. The parotid may also be affected.

In mixed forms of dip^htheria both the cervical and submax~~illary~~^{illary} glands are affected, and in severe cases they form a mass with the surrounding tissues.

They are also more tender than in the pure form. In this type also the inflammation may go on to suppuration; but suppuration rarely, if ever, occurs in the pure type. It is present in about 1 % of all cases. The urine may be practically normal. It is often diminished; and sometimes, though rarely, suppressed.

Albumen is present in about half the cases; but if the cases are treated early it will be absent in more than half of them. It depends upon the toxæmia; so that, if that be prevented by early treatment, albuminuria will be less frequent.

It may be present on the first days, but is more usually first observed on the third or fourth days. As a rule it persists for 3 to 10 days.

It is usually more frequent and abundant in the mixed than in the pure type of the disease.

Oedema is rare in diph^htheria, and, when present, is generally limited to the face. There may be hæmaturia. Occasionally hyaline or granular casts or renal cells are present in the urine.

COMPLICATIONS AND SEQUELAE:- Paralysis, although usually considered as a sequela, may occur early in the disease. When occurring early it usually affects the velum palati. The voice becomes nasal, and fluid regurgitates through the nose;

swallowing, especially of fluid, is difficult, the food tending to pass into the trachea. As a rule the paralysis is bi-lateral, but sometimes it is unilateral, the uvula being drawn to one side. The whole or half the velum is immovable, and the palatal reflexes may be absent.

According to Baginsky, when the paralysis occurs early it is due to the disease involving the muscle itself, as the paralysis occurs in that part immediately affected by the pseudo-membrane. But paralysis as a rule occurs during convalescence or later. The degree of paralysis does not appear to be necessarily related to the severity of the primary disease, as some of the worst cases are met with after mild attacks. Often the attack has been so mild that the patient first consults his medical attendant for the paralysis, when the attack has to be diagnosed from the paralysis alone.

In this case a swab from the throat may confirm the diagnosis. But paralytic symptoms, when they do occur, are apt to develop earlier after a severe attack, and are usually more severe.

They also occur more frequently after a severe than after a mild attack. The paralysis depends upon the amount of toxin in the system.

In Lennox Browne's 1,000 cases paralysis occurred in 14 %.

Sanné reports 11 % in 2,400 cases treated with antitoxin. The onset of paralysis is usually gradual and is at first limited in distribution. It may remain localized or gradually become general. After the palate the muscles of the pharynx and larynx are affected, causing difficulty in swallowing, and leading to the passage of fluids into the glottis.

Next to these the eye muscles are most often affected. There is often hypermetropia rarely myopia -- from paralysis of the ciliary muscles; the loss of accommodation being usually bi-lateral. The pupils may have a sluggish reaction to light. Convergent strabismus is often seen. Ptosis is seen less frequently.

Sometimes, though rarely, there is complete ophthalmoplegia of both eyes.

Slight ~~facial~~ paralysis may be sometimes seen. The limbs and trunk are often paralysed, paralysis of the lower limbs being sometimes an early symptom.

Formication, numbness, hyperaesthesia, and neuralgia may precede the paralysis in the parts about to be paralysed. The paralysis may be both sensory and motor. This is well seen when the muscles are being treated with electricity. The paralysis is usually bi-lateral, and the legs commonly suffer before the arms.

During one small epidemic the writer had one case where the paralysis affected the right side alone, both right arm and right leg being affected; and ~~the~~ another case, which was bilateral, in which the arms were affected before the legs.

At first the gait becomes unsteady, and as the paralysis increases, the limbs become useless and the muscles wasted. Faradic irritability is gradually lost, but the galvanic is usually retained. There may be anaesthesia of the extremities. The patellar reflex is lost, but the loss is often preceded by exaggeration, when ~~ankle~~ clonus may also be present.

When the muscles of the upper extremities are affected it is first shown by awkwardness in the use of the arms and hands. This may go on to complete loss of power.

When the paralysis becomes more general the back and neck may be affected; the head falls on the chest, and the patient may be helpless.

There may be also loss of control of the bladder and rectum. The intercostal muscles are sometimes affected; if unilateral, the ~~respiratory~~ respiratory movements of the affected side are diminished or lost; if bi-lateral, the entire thorax is immovable during respiration.

Paralysis of the diaphragm sometimes occurs, and is of serious import, as it is usually assoc-

iated with symptoms of heart failure.

It may come on insidiously or develop quite suddenly as part of a cardio-pulmonary crisis.

The symptoms are depression of the abdomen during inspiration and bulging during expiration, accompanied by rapid and panting respiration.

Cardiac complications often occur in diphtheria. There is always some feebleness of the heart's action as part of the general asthenia.

But often cardiac failure occurs. Of 3,384 cases of diphtheria collected by the American Pediatric Society cardiac failure occurred 32 times -- all fatal, the average day of the disease being the seventh; earliest, second; latest, thirty-sixth.

Cardiac failure may be due to the direct action of the poison on the heart or to changes in the vagus. It is very difficult to differentiate the symptoms due to the heart itself and those due to the nervous supply. Both the heart and the nerves may have a part in the failure.

Failure may be gradual; the pulse becomes gradually but rapidly weaker; the heart sounds, especially the first, become weaker.

The pulse becomes rapid or slow and irregular. Sometimes there are systolic murmurs at the apex with reduplication of the second sound. The face becomes extremely pale, and there is profound prostration. The skin becomes cold and clammy.

The temperature gradually falls and becomes subnormal. Sometimes cardiac paralysis occurs suddenly without warning and fatal syncope occurs.

In an intense form cardiac paralysis is ushered by nausea and vomiting, with cardiac distress and dyspnoea, and abdominal pains.

The symptoms resemble the more gradual form; the breathing becomes laboured; the pulse becomes quick, small, feeble, and intermittent, but it may become slow. The body becomes pale, blue, and cold; and this is followed by death.

Respiratory Complications are always grave in diphtheria. Bronchopneumonia is by far the commonest. Of 3,384 cases of diphtheria reported by the American Pediatric Society, bronchopneumonia occurred in 5.9 %. It is apt to follow laryngeal cases. As to the cause there is much disagreement amongst authorities.

By most it is attributed to the action of the streptococcus alone or with other organisms.

Kanthack and Stephens believe that it is caused by the diphtheria bacillus. Woodhead and others have found the diphtheria bacillus seldom if at all; but have found the streptococcus, staphylococcus, and pneumococcus. It seems to be due to more than one organism, those most frequently present being the streptococcus pyogenes and diphtheria bacillus, generally in combination.

Bronchopneumonia comes on with an increase in temperature, pulse, and respiration. When following laryngeal diphtheria the cyanosis and dyspnoea, if present, are increased.

The ratio of respiration to pulse is also increased. Also the usual signs of bronchopneumonia develop.

Lobar pneumonia may also, though rarely, occur. Bronchitis occurs frequently, especially after laryngeal cases, when the symptoms of bronchitis are super-added to those of diphtheria.

Other rarer respiratory complications are emphysema, collapse of lungs, pulmonary apoplexy, abscesses of lung, and empyema.

Septic pneumonia may occur from paralysis of the laryngeal muscles allowing the entrance of septic matter into the lungs; also after tracheotomy.

Various Skin Lesions may also complicate diphtheria -- especially the mixed forms of it: e.g., urticaria, erythema, measly and scarlatiniform rashes. The injection of antitoxin is sometimes followed by a well marked rash; e.g., ~~urticaria~~ urticaria, erythema, scarlatiniform, measly.

They are probably due to the serum and not to the antitoxin.

In septic diphtheria there may be purpura. Joint pains with serous or purulent effusion may also complicate diphtheria, especially the complex

type. These pains and swellings are apt to follow antitoxin treatment.

LARYNGEAL DIPHTHERIA. This occurs usually, though not exclusively, in children. It may occur primarily, but as a rule it is due to downward extension from the throat. In rare cases it is caused by upward extension from the bronchi and trachea.

When primary the prodromal symptoms may be similar to those described under diphtheria of the throat. When secondary to diphtheria of the fauces it begins to show itself from the third to the sixth day. The course of the disease is usually divided into three stages, though there is no hard and fast line between the different stages:-

- (1). Stage of invasion.
- (2). Stage of spasm.
- (3). Stage of asphyxia.

(1). There is hoarseness of voice, with a short, dry, metallic cough. This stage lasts a day or two usually. It is succeeded by

- (2). a change in the voice and dyspnoea.

There follows partial and complete aphonia. The cough becomes dry and hoarse, and occurs in paroxysms, lasting from one to several minutes.

There may be long intervals between the paroxysms; but as the disease progresses the intervals become shorter. The pulse gets more frequent and small. During a paroxysm the patient is in great distress and clutches at his throat; the

face becomes livid, the veins about the head and neck bulge, the head and face are covered with sweat. The respiration becomes harsh *and* strident. Inspiration is attended by wheezing.

Respiration is increased in frequency. During the dyspnoea all the accessory muscles of respiration come into play; there are depressions at the supra-clavicular regions, neck, and epigastrium.

Between the attacks the patient lies exhausted, covered with sweat. The attack may be relieved by the coughing up of false membrane or mucus.

If the disease progresses this leads to
(3). Asphyxia.

Respiration becomes more rapid and then irregular. The inspiratory recessions become more marked. Cyanosis deepens. There is extreme restlessness.

This gives place to apathy and stupor as the suffocation advances. Death occurs by stupor, or coma, or by convulsions. During the third stage there is often seen great pallor of the body and a partial or complete loss of the radial pulse during inspiration. These are supposed to be due to the production of a vacuum in the thorax, which causes the blood to enter the intrathoracic vessels, which in its turn leads to depletion of the peripheral vessels. Where a laryngoscopic examination is possible there is seen at the onset of the disease redness and swelling of the mucous membrane of the

larynx. Later membrane in various stages may be seen on the epiglottis, vocal chords and the trachea.

But even at this stage membrane may be absent. When the attack is primary the diagnosis may be confirmed by a swab from the throat as low down as possible.

There are various theories as to the cause of the dyspnoea:-

- (1). Bretonneau's -- mechanical obstruction due to the false membrane.
- (2). *Jurine's* -- spasm of the glottis.
- (3). Neimeier's -- paralysis of the dilator muscles of the glottis.
- (4). Cadet de Gassicourt's -- excitation of respiratory centres by carbonic acid poisoning, and reflex action of the vagus nerve.

The most common opinion is that it is due to both spasm and the presence of false membrane.

Diphtheria of the bronchi is not easy to diagnose the only sure sign being the coughing up of a cast of a bronchus. It may show itself by loss of respiratory sounds over a particular lung area especially after tracheotomy or intubation.

The breathing ~~is~~ is very rapid, and there are no spasms, unless the larynx is involved, the dyspnoea being continuous. There is extreme prostration also.

Nasal diphtheria is usually secondary to pharyngeal diphtheria. Rarely it is primary, especially in the newborn. Of Lennox Browne's 1,000 cases two only were primary and 211 secondary.

It is characterized by block~~ing~~ of the nostrils, and by a thin, sanious, offensive, irritating, discharge, causing much excoriation of the upper lip and nostrils. There is great weakness and signs of extreme toxæmia.

Epistaxis is apt to occur and maybe severe. Respiration is snuffling in character and more or less oral. In babies there is diff~~icult~~ty in taking the breast. The mucous membrane may be seen red and swollen, or later membrane may be seen on the septum or deeper in the canal. Membrane may be removed by forceps. Where there is complete occlusion of the nose death may be by suffocation or toxæmia. Where the membrane is not distinct enough to justify a positive diagnosis recourse should be had to bacteriology.

Nasal diphtheria is sometimes a purely local disease with no constitutional symptoms.

Dr. D. S. Davies of Bristol reports two such cases, in which portions of membrane from the nose were found by Dawson and Klein to contain highly virulent bacteria when tested by inoculation of guinea-pigs. Nasal diphtheria may ~~also~~ also take

on a phlegmonous form when due to other organisms besides the specific bacillus.

Here the membrane is of a darker colour, and there is greater swelling of the cervical and sub-maxillary glands, and free epistaxis.

It may also occur in a septic form.

Todd describes an external variety of nasal diphtheria occurring in children convalescent from scarlet fever. It is characterized by redness at the posterior margin of one or both nostrils, becoming gradually more intense, until ultimately a moist granular-looking raw surface results.

There is no membrane, but the Klebs-Loeffler bacillus is present in the nostrils. The bacilli are supposed to be of low virulence, as it gives rise to no constitutional symptoms nor to faucial or laryngeal diphtheria.

Nasal Diphtheria may by extension give rise to otitis media and meningitis, and may possibly affect the conjunctivae through the lachrymal ducts.

Buccal Diphtheria is sometimes seen in severe cases of angina as an extension forwards from the throat; especially is this the case in complex diphtheria. It is rarely primary.

In Lennox Browne's 1,000 cases it occurred but once. The writer had one primary case in 150 cases of diphtheria. There was a patch of

membrane about $\frac{1}{2}$ inch square situated on the gum just below the last left molar tooth.

There was no membrane anywhere else. It was accompanied by acute nephritis with albuminuria and haematuria. Membrane is apt to form also on the interdental mucous membrane, dorsum and sides of tongue, and about the frenum.

The writer had one primary case of the hard palate.

Diphtheria of the conjunctiva occurs in three forms:- Interstitial, croupal or superficial, and catarrhal.

As a rule, it is secondary to diphtheria of the nose or other parts, but occasionally it is primary.

In all the forms the specific bacillus has been demonstrated, either alone or associated with streptococci, staphylococci, or gonococci.

The streptococcus is most often present in the first form, but the staphylococcus in the second and third forms.

The disease begins insiduously, and at first resembles a simple catarrhal conjunctivitis-the conjunctiva being congested.

As a rule the conjunctiva of the lids only is affected, though sometimes that of the bulb

also suffers. In the interstitial form there is much infiltration thickening of the lids, so that they cannot be easily everted; the conjunctiva is swollen and covered with greyish membrane which cannot be detached. After 6 to 8 days the membrane becomes disintegrated, and there is profuse purulent discharge.

This may be followed by cicatrices and adhesions. The cornea also may ulcerate and cause loss of sight.

In the croupal form the membrane is whiter in colour, and there is no infiltration and swelling of the lids. The membrane as a rule covers the conjunctival mucous surface of the lids only, and is easily detached, leaving a raw bleeding surface.

In the catarrhal form there is no membrane. It resembles catarrhal conjunctivitis; but is distinguished from it by the discharge being scanty, glairy, and thready instead of muco-purulent; by the presence of more swelling; by the conjunctiva of the bulb being less vascular and more vitreous; and by the presence of the bacillus diphtheriae.

Otitis Media may occur in diphtheria. It may be due to the bacillus diphtheriae, either alone or associated with other organisms.

It is as a rule secondary to diphtheria of the throat or nose. The symptoms are deafness,

pain in and discharge from *the ear*.

The discharge may be serous or purulent. The discharge in culture will show diphtheria bacilli seldom pure, but associated with one or more other organisms.

Membrane may be seen deep in the canal.

Diphtheria may affect other mucous membranes also; e.g., the vulva, vagina, anus, rectum, glans penis, prepuce, urethra.

It is diagnosed by the presence of false membrane and inflammatory swelling &c.

As the disease in these cases is usually secondary it is difficult to tell what part of the constitutional effect is due to the primary or secondary affection. Diphtheria of skin wounds may be diagnosed by the presence of false membrane and by bacteriology.

DIFFERENTIAL DIAGNOSIS.

The differential diagnosis of diphtheria lies between

- (1). Catarrhal conditions of the throat and larynx, and
- (2). the exudative inflammations caused by organisms other than the diphtheria bacillus.

This is rendered the more difficult, as often in such cases as resemble diphtheria,

diphtheria may be superadded to the disease.

This is especially true as regards measles and scarlet fever. In 18,328 cases of diphtheria reported by Gordon Pugh to the Metropolitan Asylums Board, 1900, 4.71 % of the cases were complicated with scarlet fever.

In 150 cases of diphtheria the writer had, one severe case was a complication of scarlet fever. The differential diagnosis of diphtheria is most difficult at the onset of the disease, before membrane has formed, and especially in those cases of catarrhal diphtheria where membrane is absent; and, also in those cases where membrane though present, is not easily seen owing to its situation, such as the posterior surface of the tonsil.

The writer had one case of diphtheria resembling quinsy, where no membrane was detected, but which was followed by paralysis of the whole body. At the onset of the attack it was quite impossible to diagnose the case as diphtheria without a bacteriological examination.

Where any doubt exists recourse should be had to bacteriology.

Catarrhal Diphtheria presents no membrane. The pharynx and tonsils are red and swollen.

Diphtheria may be suspected in such a case

if there be known diphtheria cases near the patient. Here also the presence of albuminuria should lead one to suspect diphtheria. The only certain means of diagnosis in such a case is bacteriology.

Scarlet Fever is diagnosed by its more sudden onset, accompanied by vomiting and high temperature.

In 24 hours the scarlet rash appears on the skin of the whole body.

Where a rash appears in diphtheria it is usually erythematous, and is most commonly seen on the chest and neck. As it is usually of late occurrence, other symptoms of scarlet fever will have developed and will help to distinguish it from the rash of scarlet fever.

Also if the case be diphtheria, membrane will be present (except in catarrhal diphtheria) in 24 to 48 hours.

The strawberry tongue of scarlet fever is characteristic, as is also the port wine redness of the throat. Where albumen is present in the urine, it is usually a late manifestation in scarlet fever, but is seen earlier in diphtheria.

Where membrane is present, that of scarlet fever is more yellowish than grey, and is surrounded by more intense hyperaemia than in diphtheria. It is also more pulpy than diphtheritic

membrane, and tends to crumble when pressed.

The membrane of diphtheria is more adherent, more elastic, and tougher.

Also the membrane of scarlet fever shows streptococci and staphylococci; that of diphtheria the specific bacillus.

Measles is easily differentiated from diphtheria. The danger lies where they co-exist. Faucial membrane is more exceptional in measles than in scarlet fever, but diphtheria is more often a sequel to measles than to scarlet fever.

Where membrane is present in measles one should suspect diphtheria. Coryza and congestion of the conjunctiva are preliminary symptoms of measles. When the rash appears on the fourth day of the disease the diagnosis is evident.

Koplik's spots are the best evidence of measles before the rash appears. These are bluish white spots surrounded by a red area, seen on the buccal mucous membrane and on the inside of the lips. These spots are of great value in differentiating early measles from early diphtheria, as they appear in the invasion stage of measles, where the difficulty exists.

* Aphthous Patches of the throat and mouth are usually seen at other sites than the tonsils and pharynx, and are not accompanied by symptoms of diphtheria.

Herpes of the Throat and Palate may be confounded with discrete patches of diphtheria membrane. It is usually associated with herpes of the lips. If the patient be old enough to complain of the pain, the presence of the pain which precedes and accompanies the herpes will be of great service in the differential diagnosis. Here again any doubt may be settled by bacteriology.

In Erysipelas of the Throat there is a higher temperature, greater distress, much oedema and lividity of the parts, and the skin of the neck is usually involved. Also membrane is but rarely present; and if present does not show the characters of diphtherial membrane.

Peritonsillitis and Tonsillitis may be distinguished from diphtheria by their more sudden onset, higher temperature, and especially the pain on opening the mouth and swallowing.

Peritonsillitis is, as a rule, unilateral; the tonsil is swollen and pushed forward, and the uvula is displaced. Where suppuration occurs the bursting or incision of the abscess clears the diagnosis. In acute parenchymatous and acute follicular tonsillitis the tonsil is much swollen and red. The local symptoms are similar to those of peritonsillitis, but are less severe. ~~is cleared by the suppuration present the diagnosis~~

Here also where pus is present the diagnosis is cleared by its evacuation.

Follicular tonsillitis is sometimes extremely difficult to distinguish from lacunar diphtheria.

The membrane of lacunar diphtheria is more adherent, tougher, and greyish. It also tends to spread from the tonsil. The exudate of follicular tonsillitis is not so adherent, more put^etaceous, and does not leave a bleeding surface when removed. It is also limited to the tonsil.

Moreover there is more salivation in tonsillitis, diphtheria being a drier disease.

The presence of albuminuria is a point in favour of diphtheria rather than tonsillitis, albuminuria being rare in tonsillitis.

But many cases can only be determined by bacteriology.

LARYNGEAL DIPHTHERIA. has to be differentiated from several affections of the larynx; e.g., non-bacillary membranous croup, the spasmodic form of acute laryngitis or laryngitis stridula, laryngismus stridulus, pseudo-membranous croup following measles and sometimes scarlet fever, retro-pharyngeal abscess, oedema of the larynx, syphilis of the larynx, obstruction of the larynx due to foreign bodies &c. Symptoms of croup following diphtheria of the throat may, in most

cases, be set down to diphtheria.

When croupy symptoms follow measles and scarlet fever, unless there be symptoms of throat diphtheria, they are probably due to non-diphtherial membrane. The catarrhal croup, which sometimes accompanies the onset of measles, usually subsides with the appearance of the rash.

The false membrane often present in measles has a great tendency to extend downwards to the larynx and trachea. If the membrane present in the throat be not diphtheritic, it may be presumed that that present in the larynx is of the same character.

The most difficult cases to differentiate are primary laryngeal diphtheria and other primary inflammatory lesions of the larynx.

Primary diphtheritic croup may be positively diagnosed when a swab of the throat taken as low down as possible shows the presence of the specific bacillus. But one should remember that, often in these cases, the absence of the organism does not of necessity disprove laryngeal diphtheria.

Acute spasmodic laryngitis has a more sudden onset than laryngeal diphtheria. It occurs usually at night, and tends to abate in the morning.

The dyspnoea is not so pronounced, and does not advance as steadily and rapidly as in diphtheritic croup. The remissions of the spasms are also more marked. Also with proper treatment -- purgation, diaphoretics, hot poultices &c. the attacks pass off.

Laryngeal diphtheria begins more insidiously and progresses more steadily and rapidly; it is also accompanied by more asthenia. The presence of albumen in the urine would be a strong point in favour of diphtheria.

Laryngismus Stridulus is almost invariably associated with rickets. There is absence of fever. During the intervals between the spasmodic attacks there is complete freedom from symptoms which indicate laryngeal disease, such as cough, hoarseness &c.

During the attack there is absolute cessation of respiration. There is also a history of some irritation in the alimentary tract or elsewhere, such as unsuitable diet, worms &c. With prompt treatment the attack passes off.

Non-bacillary Croup is very difficult to diagnose from the bacillary form. Some authorities, eg., Sidney Martin, maintain that there is no such disease; but others believe that there is, and that it is of more frequent occurrence than many imagine.

Billings and Lennox Browne found 14 % of membranous croup to be undoubtedly non-bacillary.

The membrane in such cases has been found to be due to streptococci, staphylococci, Vincent's spirillum, and other organisms.

The symptoms are very similar to those of laryngeal diphtheria.- But at the onset the disease is more sthenic than diphtheria.

Yet when obstruction has existed for some time, there is asthenia, due to a deficient supply of oxygen and carbonic acid poisoning.

Thus, at a late stage, nothing but a bacteriological examination can differentiate it and diphtheria.

But non-bacillary croup has a more sudden onset, the temperature is higher -- 102° to 103° , rises more rapidly, and is more persistent.

The membrane is more yellow, softer, more friable, more easily detached than the specific membrane, and does not leave a bleeding ulcerated surface when detached.

Retropharyngeal abscess is differentiated best by a digital examination. A writer in the B. M. Journal recently maintained that this is the only means of making a certain diagnosis of retropharyngeal abscess. Other symptoms are great difficulty in swallowing, fixation of the head, bulging of the pharyngeal wall.

The swelling is rarely central, the glands behind the angle of the jaw on the corresponding side being enlarged, hard, and tender.

Oedema and syphilis of the larynx, and foreign bodies in the larynx are distinguished from laryngeal diphtheria by the history of the case, by the laryngoscope, and, in the case of syphilis, by symptoms of syphilis in other parts of the body. Where any doubt exists, recourse should be had to bacteriology.

Nasal Diphtheria has to be differentiated from acute catarrhal rhinitis, acute purulent rhinitis of infants, syphilis, non-diphtheritic membranous rhinitis, glanders, foreign bodies in the nose &c.

The diagnosis of nasal diphtheria is easier when membrane can be seen in the nose. But often membrane may not have had time to form.

If membrane be not evident, it is well to remember that nasal diphtheria is, as a rule, secondary to pharyngeal diphtheria. So an examination of the throat will usually clear up the diagnosis; because the presence of pharyngeal diphtheria is strong presumptive evidence in favour of the rhinitis being diphtheritic.

But nasal diphtheria is much more difficult to diagnose when primary.

In this case it may be missed owing to the absence

of membrane, or may be wrongly diagnosed owing to the presence of membrane. In some cases it is impossible to be certain of the diagnosis without a bacteriological examination.

Acute Catarrhal Rhinitis is accompanied by sneezing, and a profuse mucous or muco-purulent discharge, the discharge being less irritating and less offensive than that of nasal diphtheria.

There is neither asthenia nor adenitis in acute rhinitis. The discharge of nasal diphtheria is scanty, foul, irritating, and is, as a rule, accompanied by swelling of the cervical and submaxillary glands.

Again, epistaxis is of frequent occurrence in nasal diphtheria; it is rare in simple rhinitis.

Acute purulent rhinitis of infants is usually caused by infection at birth.

It is characterized by redness and swelling of the mucous membrane, which is followed by purulent discharge and nasal stenosis.

No membrane is present. The microscope will show the absence of the diphtheria bacillus and the presence of other organisms, e.g., gonococci.

Syphilis of the nose can be differentiated by the history of the case, the presence of other

manifestations of syphilis, and the absence of other symptoms of diphtheria.

Non-diphtheritic membranous rhinitis is characterized by the presence of false membrane closely simulating that of nasal diphtheria.

It is due to the presence of the streptococcus pyogenes and the staphylococcus pyogenes aureus. It occurs less frequently than nasal diphtheria. The appearance of the membrane is similar to diphtheritic membrane.

The disease is characterized by the presence of this membrane blocking the nostrils, and by mucous discharge. It is a purely local disease, there being no disease of the throat or other regions. Adenitis, albuminuria, toxic symptoms, and paralytic sequelae are always absent.

It cannot be differentiated with certainty from nasal diphtheria except by a bacteriological examination.

Acute Glanders may be distinguished from nasal diphtheria by the character of the nasal discharge. In glanders this is at first, glairy; but, when the nodules ulcerate, it becomes viscid, and muco-purulent. On inspection the mucous membrane of the nose is seen to be infiltrated with nodules, which soon ulcerate and give rise to the discharge. The nose becomes red, painful,

and swollen. An eruption of papules occurs on the face and other parts of the body, which form vesicles, and finally pustules.

These symptoms are absent in nasal diphtheria. If the patient was inoculated through a wound, the wound will be red and swollen. Inspection of the nose and throat will show the absence of the characteristic signs of diphtheria.

The occupation of the patient, e.g., hostler &c., will help to differentiate.

Bacteriology will show the presence of the bacillus mallei and the absence of the bacillus diphtheriae

In chronic glanders the nasal mucous membrane is covered by dirty scabs, and there is a discharge of offensive, viscid, muco-purulent matter.

Foreign bodies in the nose can be distinguished by the history of the case, the character of the discharge, and by inspection.

A unilateral discharge is a point in favor of a foreign body.

Bacteriology will remove any doubt.

Diphtheria of the Conjunctiva has to be differentiated from acute catarrhal conjunctivitis, phlyctenular ophthalmia, gonorrhoeal ophthalmia, ophthalmia neonatorum.

The presence of diphtheria in the nose or

elsewhere is a great help in the diagnosis.

But when primary it is more difficult to differentiate. The presence of membrane on the palpebral conjunctiva serves to distinguish the interstitial and croupal from all other diseases.

As there is no membrane in the catarrhal form of conjunctival diphtheria this is more easily mistaken for acute catarrhal conjunctivitis.

Here the character of the secretions will help in the diagnosis, that of ~~d~~iphtheria being scanty and glairy, whilst that of simple conjunctivitis is more profuse and muco-purulent.

Also there is more congestion of the ocular conjunctiva with loss of lustre in the simple form) and also less swelling of the lids.

Gonorrhoeal ophthalmia is differentiated by its more rapid onset and the absence of membrane. Ophthalmia neonatorum is also distinguished by the absence of membrane. The character of the discharge will serve to distinguish both forms from the catarrhal form of conjunctival diphtheria.

Phlyctenular ophthalmia is differentiated by the presence of the characteristic ulcers on the ocular conjunctiva, and by the type of patient.

In all the above bacteriology will confirm the diagnosis by ~~w~~showing the presence of the

diphtheria bacillus or other organisms in the discharge.

TREATMENT. The treatment of diphtheria may be considered under the following heads:-

(1). Prophylaxis. (2). Hygiene. (3). Antitoxin treatment. (4). Local treatment. (5). General treatment. (6). Operative treatment.

(1). Prophylaxis. Suspected persons should be isolated until the absence of diphtheria has been demonstrated. Where the clinical evidence in favor of diphtheria is strong, it is better to treat the case as diphtheria, even before the bacteriological evidence can be got.

All diphtheric patients should be isolated until the Klebs-Loeffler bacillus has disappeared from the throat and nose. This can be determined by a bacteriological examination only.

The time that elapses between the disappearance of the false membrane and the disappearance of the bacilli varies from 6 days to 9 weeks.

There are records of some rare cases where the bacilli persisted for 9 months.

Antitoxin seems to have no influence upon the persistence of the bacilli.

The room should be cleared of carpets,

hangings, rugs, furniture &c., and only such things as are absolutely necessary should be left.

It should be well ventilated, and have as much sunlight as possible. A sheet wrung out of an antiseptic fluid should be hung over the doorway.

The sick attendant should communicate as little as possible with others, and no one else should be admitted into the room.

He should also wash his hands in an antiseptic fluid after making local applications to the throat and before eating.. The discharges should be received into antiseptic solutions, such as Jeye's Fluid. Old linen rags, which can be burnt, should be substituted for handkerchiefs.

Eating vessels &c., should be kept apart for the patient, and after use, should be washed in an antiseptic fluid, and then in clean water.

The sick room should be washed occasionally with an antiseptic fluid such as Jeye's.

The attendant should insufflate ~~his throat~~ his throat with sulphur every 4 hours. If the patient happens to cough on his face or eye, the attendant should immediately wash the part in an antiseptic fluid, such as corrosive sublimate, 1 in 2,000 or so.

The medical attendant also should take the same precautions in making his visits.

The question that naturally arises here is

whether those in contact with diphtheria patients should be immunized with antitoxin.

Northrup and others strongly advise it, but others disapprove of it. The writer is inclined to adopt the latter view, for the following reasons:-

- (1). With reasonable care, diphtheria can be avoided, as it is not contagious to the same degree as some other diseases, such as scarlet fever and measles.
- (2). The immunity gained with antitoxin is of but short duration, averaging 4 weeks.
- (3). Antitoxin is not as free from danger as was thought some time ago. Klotz, in the September 1907 issue of the Montreal Medical Journal gives some cases where death followed the injection of serum: Death in some instances took place in from 5 to 15 minutes after injection. The symptoms are collapse, unconsciousness, convulsions, death.

Amongst the cases quoted is that of Professor Langh~~an~~^{an}'s 2 year old son, who was given 1.3 c. cm of serum as a prophylactic measure, and died ten minutes afterwards.

At the autopsy no abnormal conditions were found save vomitus in the respiratory tract.

- (4). Antitoxin, if given on the first day of the disease, is nearly always successful.

On the first sign of throat trouble a suitable dose of antitoxin should be administered.

At the termination of the case the attendants should disinfect their clothes and persons.

The room should also be thoroughly disinfected. The walls, ceiling, and floor should be washed with a solution of Jeye's fluid &c.

Some recommend rubbing the walls and ceiling with bread. Carpets, clothes &c., should be put in linen soaked in an antiseptic fluid and taken away to be steamed. It is advisable to scrape the paper from the walls. The room should then be damped, all holes plugged, and sulphur burnt and left for 24 hours.

A pound of sulphur to each 1,000 cubic feet is advisable. Some authorities recommend the vapour of other antiseptics, such as formaldehyde.

Immersion of the furniture in boiling naphtha is recommended by Retch, as the boiling point of ϕ naphtha is lower than that of glue.

Finally the patient's whole body should be washed at the termination of the illness, special attention being paid to the hair. He should then be dressed in clothes which are free from contagion.

(2). Hygiene. But little can be added to what has just been said. In addition to having good ventilation and sunlight, the room should be properly warmed, having a temperature of about 64° F.

(3). Antitoxin treatment.

By this is usually meant the treatment of diphtheria by injecting under the skin of the patient the serum of animals which have been rendered artificially immune to diphtheria. But the serum can be given also by mouth or rectum.

The serum used is that of horses which have been rendered immune by repeated injections of diphtheria toxin.

This toxin is obtained by growing virulent cultures of diphtheria bacilli in bouillon.

The culture is sterilized by the addition of 5 % carbolic acid, and filtered. With this toxin several horses are injected, at intervals, with increasing doses, until their blood is found to contain serum of a sufficiently high degree of antitoxic power.

The antitoxic strength of the serum is estimated by inoculation of guinea-pigs with a mixture of toxin and antitoxin.

Thus a normal unit is found, which Park defines as "that amount of antitoxin which is required to neutralize sufficient toxin to kill 100 small guinea-pigs. This amount of poison is produced by the growth for one week of a virulent bacillus in 1 c. c. of bouillon".

The antitoxin treatment of diphtheria is the most efficacious treatment known, and has reduced

the mortality about 50 %. There is no doubt that, in course of time, the mortality will be further reduced. The mortality after tracheotomy has also been reduced by about 50 %. The remedy is of the greatest value in those cases* which, with other modes of treatment, give the worst results, that is, in the very young, and in laryngeal cases.

There is also a great diminution in the cases that require tracheotomy.

Of 27,210 cases treated without antitoxin in the four years 1891 to 1894 by the New York Board of Health the mortality averaged 34.9 %.

Of 34,673 cases treated with antitoxin in the four years 1897 to 1900 the mortality averaged 13.6 %. The superiority of the antitoxin treatment over other modes of treatment is shown upon the mortality in the very young. Biggs and Guerard report a mortality of 31.4 % ⁱⁿ antitoxin cases occurring from 0 -- 2 years, and 6.9 % in cases occurring over 10 years.

Baginsky reports in cases treated without antitoxin a mortality of 63.3 % occurring from 0 -- 2 years, and 14.6 % occurring after 10 years.

On eye cases the effect of antitoxin is most gratifying. . McCullom reports 15 cases of conjunctival diphtheria successfully treated with antitoxin, in all of which the eye would have been lost without antitoxin.

On paralysis the effect of antitoxin will vary according to the stage of the disease in which it is given. If used early it will undoubtedly tend to prevent paralysis.

But, if used late, it will show an increase in the frequency of paralysis; as many severe cases which would have died before the onset of paralysis, after antitoxin injections, live to develop nerve lesions.

If much toxin has developed before the administration of antitoxin paralysis is likely to occur. But even, in that case, the later forms of paralysis will be prevented, or favourably modified.

As regards the effect of antitoxin on the kidneys, authorities differ. Some assert that antitoxin tends to prevent nephritis and albuminuria. Others say that it increases their frequency. There is very likely a slight transient albuminuria due to the serum. The consensus of opinion is that it has no practical effect on the kidneys.

On heart and other complications, antitoxin, if administered early in the disease, has undoubtedly a very beneficial effect.

Two essential conditions of success with antitoxin are:-

(1). To give it early in the disease, and

(2). To give a sufficient dose.

These two conditions have a direct effect on each other, as the dose should be regulated by the stage of the disease in which it is given.

To obtain the same effect it will require as much twenty times on the fourth day of the disease as it would on the first day. As regards the time to give it -- the sooner the better.

The dose should be regulated by the age of the patient, the severity of the disease, and the stage of the disease.

Each case should be judged on its merits. It is better to give too much than too little. There is no doubt that too small a dose was given when antitoxin was first used. Where we now know that 5,000 units are necessary as little as 500 units were thought to be sufficient. Now for children^{of} 6 -- 10 years, 6,000 to 8,000 units are injected, and this dose has been found sufficient.

McCollom recommends 2,000 to 4,000 units. Northrup advises 2,000 to 3,000 units for a child of over a year in an ordinary case of diphtheria; from 3,000 to 5,000 units in severe cases and in all laryngeal cases, of any age; 1,500 to 2,000 units for a child under one year in an ordinary case. The writer had a child of 18 months, who did well with 1,000 units followed in 12 hours by

500 units.

The dose should be repeated if no improvement follows in 12 to 24 hours, and again in 24 hours if necessary.

The writer had one very severe throat case in a child of 4 years, in which a dose of 6,000 units had to be repeated at intervals of 5 days, until 24,000 units had been injected. Each injection was followed by a decided improvement lasting 3 days; then followed a relapse, until the next injection was given. The child improved steadily after the fourth injection, and made a good recovery.

It is important to have fresh serum, as it is proved to lose 50 % of its antitoxic power in 12 months. As serum itself sometimes has a harmful effect, it is better to use the antitoxic serum in a concentrated form. No special syringe is necessary. Many forms are used. It is necessary to have one that can be rendered aseptic by boiling. The needle of the syringe should be small

The serum may be injected under the skin of the abdomen, flank &c. The part should be rendered aseptic by soap and water, followed by an antiseptic such as bichloride solution &c.

The injection should be made slowly and the part covered by an antiseptic pad of any suitable material held in place by plaster.

The injection is followed by a local swelling, slight redness, and pain, which soon pass off.

The beneficial result of the injection is indicated by a marked amelioration in the local and general symptoms, and by its characteristic effect upon the false membrane.

In this connection it should be remembered that in most cases the injection is followed in 4 or 5 hours by a rise in the temperature of 1° to 2° , and by acceleration of the pulse.

The rise of temperature lasts but a few hours, but the acceleration of pulse is apt to persist longer. This is probably due to the serum, and not to the antitoxin, as it is known to follow non-immunized serum.

In favourable cases, especially in pure diphtheria, the patient, in about 24 hours, has a brighter appearance; the constitutional symptoms improve; the faucial swelling subsides, and the swelling of the cervical glands diminishes.

Nasal discharge, if present, diminishes rapidly, and finally disappears.

In pure diphtheria, the temperature falls rapidly, and becomes normal in 2 or 3 days. The pulse also improves gradually, according to the fall of temperature. In mixed diphtheria the temperature falls more by lysis.

In a few hours, the false membrane whitens, shrinks, becomes rolled up at the edges, ceases to spread and finally becomes detached, either in small pieces, or en masse. This change in the membrane is accompanied by congestion and swelling of the mucous membrane surrounding it. Certain rashes often follow the injection of antitoxin.

Authorities differ as to their frequency, the average being about 20 %. The rashes are often accompanied by fever, joint pains, sickness, vomiting, and diarrhoea.

The rash may ^{be} erythematous, ^{urticarial} scarlatiniform, morbilliform, petechial. It may occur from the second to the 12th day. It lasts usually about 2 days. In the B. M. Journal, Feb. 29th 1908, Dr. Bligh, Caterham Valley, reports his own case. In his case the injection was followed on the 9th day by a severe attack of urticaria, lasting but a few hours.

As a preventive for the rash he recommends the administration of calcium chloride or lactate for 9 days, commencing a day or two after the injection.

The rash is often followed by desquamation, which, according to Berg, resembles that of measles. The various rashes are due to the serum. This has been proved by experiments with non-immunized serum.

Of the chemical nature of antitoxins little is known. From their experiments, C. J. Mark and Cherry deduce that while toxins are of the nature of albumoses, the antitoxins probably have a molecule of greater size, and may be allied to the globulines.

This may explain Sir Thomas Fraser's observation "that it requires 10 to 20 times as much antitoxin to neutralize a certain dose of toxin, when both are injected at different sites subcutaneously, as it does when the toxin is injected subcutaneously and the antitoxin intravenously".

This may be due to the antitoxin being absorbed more slowly than the toxin owing to its molecule being the bigger of the two. (Muir and Ritchie).

The mode of action of antitoxin is not definitely known. Ehrlich's lateral chain theory is now mostly accepted. He supposes that there normally exist in the cells of an animal capable of supplying antitoxin certain atom groups which are capable of combining with the toxin molecule.

When a toxin is injected in relatively small doses, the toxin combines with these atom groups, and their physiological function in the cell economy is lost. There then occurs a regeneration of new molecules to take up this function, and

when these are used up by fresh toxin molecules introduced a further regeneration takes place.

Ultimately there occurs an over-regeneration, and the appearance of these molecules (antitoxin) in the blood. (Muir and Ritchie).

Antitoxin treatment should be adopted in every case of diphtheria.

Local Treatment:-

This has for its object:

- (1). The destruction of the bacilli, thereby causing a cessation of the inflammation, and preventing extension of the membrane; and
- (2). The prevention of toxic absorption, and removal of membrane and the products of decomposition.

For these objects various methods have been advocated. Forcible removal of membrane, except in the case of nasal diphtheria, is now condemned.

Various substances are recommended with the object of destroying the bacilli. Jacobi recommends touching the membrane once or twice a day with a 50 % carbolic acid solution in glycerine, solution of 1 to 100 or 1 to 500 bichloride of mercury. Loeffler recommends applying to the affected part, twice in succession for 10 seconds, a cotton tampon steeped in a solution of iron, toluol, and creolin; this to be repeated

every 3 hours until all local symptoms have disappeared. Lennox Browne recommended touching the membrane once or twice a day with pure lactic acid, and every 4 hours with diluted (1 to 4) lactic acid.

The perchloride and sesquichloride of iron are also recommended. The writer has used sublimed sulphur for many years, and is well satisfied with it. It is found, if used early in the disease, to abort it. The important point in the treatment is to apply it often enough. For this purpose it is ordered to be insufflated every hour until the temperature has fallen to normal.

Diet and medicine are to precede immediately each insufflation. By these means the sulphur is kept continually applied to the throat.

No other local treatment is used. Even without antitoxin the throat is generally free from membrane in 2 to 4 days.

Antimicrobial diphtheria serum is also recommended for local application to the throat. Many other local remedies have been recommended, e.g., guaiacol, chlorine water, resorcine, peroxide of hydrogen &c. The most common form of local treatment in use now is nasal irrigation with a warm solution of common salt or a weak antiseptic.

It is said to be very comforting. It is used by means of a fountain syringe for the nose or throat -- a smaller nozzle being used for

the former than the latter.

The child usually lies on his side, and water is made to pass up one nostril and down the other.

It is used similarly for the throat. The irrigation is repeated every 3 or 4 hours. The temperature is from 110° F to 130° F.

When the cervical glands are swollen and painful much benefit may be derived from cold applications by means of ice bags or Leiter's coils.

Some prefer hot poultices frequently changed. These hot or cold applications reduce the inflammation and cause separation of the membrane.

GENERAL TREATMENT:- Here our object is to maintain the strength of the patient, to help the system to rid itself of the toxic products, and to combat the effects of the poison on the system by treating the constitutional symptoms attributable to it.

The patient should be put to bed in a warm, light, well ventilated room, as mentioned before.

He should be kept in bed until all dangers of complications has passed. All unnecessary exertion on the part of the patient should be avoided. The diet should be light and nutritious. If the tongue be clean there is no objection to light easily digested soft solids, such as bread and

milk, milk puddings, custards, jellies &c.

Milk should be the chief article of diet. It should be given often, every 2 or 3 hours, according to the quantity taken at a time.

Beef tea, Brand's Essence, Valentine's Meat Juice &c. should also be given. Sometimes, if there be paralysis of the palate, or in intubated cases, the food must be given by the stomach tube either through the nose or mouth.

The bowels should be attended to. If there be constipation, a sharp purge at the commencement of the disease is beneficial.

Of treatment by drugs there is not much to say. The writer in an ordinary case, gives a mixture of Liquor Ferri Perchloridi and Chlorate of Potash as a routine treatment. The iron has a beneficial effect on the blood. Probably the local action of the mixture on the throat has more to do with its good effect than its constitutional action. It is given every hour, each dose being followed by insufflation of sulphur.

Where there is a diminution in the quantity of urine Liquor Ammonii Acetatis is substituted for the Chlorate of Potash. The beneficial effect of the latter mixture is increased by the frequent application of hot poultices to the loins. Sometimes, where suppression of urine threatens, the iron mixture is replaced by a

mixture of acetate of ammonia, spiritus aetheris nitrosi, and digitalis, given every 3 hours until the danger passes. If cardiac failure threaten strychnine and digitalis are of service, or strychnine alone. Many authorities speak highly of alcohol for cardiac depression. If used, it is best given in the form of whiskey or brandy well diluted with water; beginning with small doses, 15 or 30 drops every 2 hours, and going on to 2 drams every 4 hours for a child of two years. The dose should be regulated by its effect on the pulse.

The treatment of the cardiac crises is almost hopeless. Strychnine may be tried, either by mouth or hypodermically; also electricity, and inhalation of oxygen. The writer had three cases of cardiac paralysis in which treatment had no effect whatever. The paralytic sequelae are best treated by prolonged rest in bed and electricity, either the galvanic or faradic. Later, exercise is of benefit. The electricity must be used perseveringly, as it usually takes a long time to effect a cure. Here also iron, strychnine, and phosphorus are of great value. The writer had two cases treated as above, in which the good effect of electricity was most marked. In both cases the faradic current was used.

Operative Treatment:- This has for its object

the relief of the symptoms of progressive dyspnoea which are caused by stenosis of the throat or larynx. The obstruction may be caused:-

- (1). By enlarged, inflamed, swollen tonsils and uvula, and
- (2). By laryngeal stenosis.

So some authorities, e.g. Lennox Browne, Bouchet, Lefferts, Macintyre of Glasgow -- advocate removal of the tonsils and uvula in acute diphtheria, if the dyspnoea is caused by them. They have seen nothing but good following the procedure.

Many advantages are claimed for the operation of which the following may be mentioned:-

- (1). It relieves the obstruction to respiration.
- (2). As the disease is often limited to the tonsils, it removes the specific bacilli, by cutting away the infected area.
- (3). It increases the effect of local treatment.
- (4). It prevents the downward progress of the membrane, and may thus be the means of averting the necessity of intubation or tracheotomy.

Sanné condemns the operation.

A month ago the writer had two cases where the operation seemed suitable, but 8,000 units of antitoxin so improved the patients that it was deemed unnecessary.

If possible, one would be inclined to defer

the operation until the recovery of the patient.

Intubation and Tracheotomy:-

These two operations are performed for the purpose of alleviating the progressive dyspnoea due to stenosis of the larynx.

Before resorting to them one should, in addition to the treatment indicated for diphtheria of the throat, use such general treatment as is specially suitable for laryngeal diphtheria.

For this purpose, after antitoxin has been promptly administered, some authorities recommend an emetic, especially at the beginning of the disease, before there are asthenic symptoms.

A teaspoonful of ipecacuanha wine is given every 15 minutes until vomiting occurs. If there be asthenia it is better not to give it.

Jacobi recommends calomel fumigations; but this treatment is not much used now.

A steam bed used to be often employed, but is not much used now. Inhalations of steam at intervals of 2 or 3 hours are much praised by some authorities. The steam is often medicated with carbonate of soda, eucalyptus oil, pinol &c.

Hot poultices, applied to the larynx, are often of service to allay the spasm and relieve the pain; but some prefer the application of cold.

When these fail to give relief in 12 to 24 hours, or when the symptoms are urgent, one should wait no longer before operating. The chief dangers of deferring operation too long are oedema of the lungs, exhaustion of the heart, and thrombosis of the pulmonary artery.

The indications for intubation and tracheotomy are similar, although some cases are more suitable for the one than the other.

The symptoms which call for operation are rapid, urgent, dyspnoea, localized to the larynx; loss of voice; stridor; respiratory recession of the epigastric and infra-costal regions, and, later on, of the supra-sternal and supra-clavicular regions; dilatation of the alae nasi; increased exhaustion; increasing cyanosis; great restlessness; failing pulse, especially if absent at the wrist during inspiration.

Favorable conditions for operation are:- sudden onset of the symptoms; resonance at the bases of the lungs; vesicular breathing; face suffused, but not dusky; eyes bright; and warm extremities. Here the membrane is probably limited to the larynx, and the chances of success are great.

Unfavorable conditions are:- less marked suction on inspiration, especially

above; slow and continuous progress of the dyspnoea; leaden hue of face, and cold extremities.

Here the membrane has probably invaded the smaller bronchi, so that the hope of success is less.

The tubes used for the intubation of the larynx are Dr. O'Dwyer's' of New York. The tubes are made of gilt metal, and vary in length from $1\frac{1}{2}$ inch to $2\frac{1}{2}$ inch for children of different ages. The tube in situ reaches within an inch of the bifurcation of the trachea. It is shaped so as to suit the configuration of the larynx. It is retained in position by having upon it a lateral bulging.

The head has a swell upon it, but its anterior part is cut off. There is a hole in the left side of the head, into which a string is inserted. Each tube has an obturator, which fits into the introducer. The tube is inserted into the larynx by means of an introducer which fits the obturator. It is removed from the larynx by means of an extractor. As they belong to the domain of surgery, a description of intubation and tracheotomy would be out of place here.

After a successful intubation of the larynx the child coughs violently a few times. The larynx and trachea soon tolerate the tube, the urgent dyspnoea is immediately relieved, the

patient generally dropping off into a calm sleep.

The whole aspect of the child is changed. According to Northrup, the average time for which the tube should be left in the larynx is 5 days for a child of 2 years. Other authorities leave it for a shorter period. In any case it should not be worn without removal for more than 5 days.

With antitoxin the longer use of the tube generally does away with the necessity for re-intubation.

J. C. Connell advises removal of the tube in 36 to 48 hours, as then, after antitoxin, false membrane becomes loosened and tends to block the tube. Blocking of the tube by loose membrane is a sign for prompt extubation.

According to Northrup the signs of loose membrane are:-

- (1). Croupy cough (the tube being in).
- (2). Flapping sound.
- (3). Sudden obstruction of outgoing air, especially during coughing. Northrup advises giving a few drops of whiskey and water in equal parts to stimulate the cough, and thus clear the tube of membrane and mucus. The tube, when blocked, is often coughed up. Watson Williams advises removal and cleaning of the tube at least once every other day. Northrup advises giving the patient gr. $\frac{1}{16}$ to gr. $\frac{1}{12}$ Morphine Sulphate a short

time before removal of the tube, in order to avoid spasm; and if dyspnoea tends to recur, to apply hot poultices to the larynx.

An intubated patient will sometimes take food in the ordinary way. Semi solids are the most easily taken. Where there is difficulty in feeding Northrup advises Casselberry's position, i.e. with the head lowered. The child is allowed to gulp several times before assuming the upright position. Others advise feeding with the child lying on its stomach. Some cases will require to be fed by means of the tube, either through the nose or mouth.

Rectal feeding is not much recommended in these cases, and, as a rule, is not very successful. The food should be given about every 2 hours. After tracheotomy, in favorable cases, there is a slight rise of temperature, lasting from 2 to 3 days.

When tracheotomy has been performed great care should be exercised in the after treatment.

A constant atmosphere of steam is now not much favoured. When the secretions are dry and viscid it is advisable to spray for 5 or 10 minutes around the cannula, either with pure steam, or with steam charged with bicarbonate of soda.

This should be done at intervals varying according to the relief obtained.

Or the soda solution may be applied to the larynx with a laryngeal brush, feather, or a bit of sponge, twisted securely into a loop of wire.

The inner tube should be kept clear by means of narrow pheasant feathers, which should be twisted round inside it before removal. The inner tube should be removed and cleaned every hour or two at first. The outer tube should be removed once in 24 hours, the wound being thoroughly cleansed at the same time.

The tracheotomy tube, after antitoxin, can generally be dispensed with in 2 or 3 days. In the pre-antitoxin days it had to be retained for from 4 to 9 days. Sometimes after removal of the tracheotomy tube, intubation is advisable for a short period.

The feeding, after tracheotomy, is similar to an intubated case, except that Casselberry's position is not advisable.

It is difficult to compare the relative merits of intubation and tracheotomy, as surgeons seem to prefer the one in which they have had the more experience. Thus most English surgeons prefer tracheotomy, whilst the American surgeons prefer intubation.

The following advantages are claimed for intubation:-

(1). It is simple and painless.

- (2). It is bloodless, and thus less terrifying, and thus permission to perform it is easily obtained.
- (3). In children under 5 years the percentage of recoveries is considerably higher than after tracheotomy, while above this age the percentage of recoveries is about the same.
- (4). It can be performed without an anaesthetic or trained assistants.
- (5). The respired air passes through the natural passages.
- (6). The intubation tube is much more comfortable to the patient than a tracheotomy tube, being hardly felt.
- (7). Coughing is more effectual -- the expectoration being more easily performed.
- (8). The after care of an intubated patient is less troublesome than that of the tracheotomized.

For tracheotomy the following are some of the advantages claimed:-

- (1). It is easier than intubation.
- (2). It is more certain of affording relief than intubation -- it being often required after intubation.
- (3). It is easier to nourish the patient after tracheotomy than intubation.

- (4). A nurse can remove and clean the inner tube whereas it requires skilled hands to remove the tube after intubation.
- (5). Tracheotomy gives functional rest to the larynx, and affords a better drainage to the trachea.
- (6). It enables local treatment to be carried out.

The following conditions leave no choice between the two operations;- tracheotomy being the one indicated:-

- (1). Great oedema of the larynx, preventing the performance of intubation, or causing it to be ineffectual.
- (2). Failure of relief after intubation owing to extensive involvement of the naso-pharynx.
- (3). The presence of membrane low down in the trachea.
- (4). Ignorance of the operation of intubation, or the absence of instruments, tubes &c.

O'Dwyer always recommended tracheotomy in preference to intubation by uneducated fingers. He asserted also that no one should attempt intubation before practising it upon the cadaver.

Experience has shown many of the objections to intubation to be groundless. Thus food can be given by the ^{stomach} tube. Also where the tube tends to block, it is usually coughed up by the patient.

Probably, as the antitoxin treatment becomes more general and perfect, intubation will become more common, as the period of dyspnoea will thereby become shorter. So intubation will be undertaken as soon as obstruction becomes manifest, and tracheotomy will tend to be confined to extreme cases only. There is not much to add as regards treatment of diphtheria at different sites. Antitoxin should be given in all cases.

In Eye cases a full dose should be given at once, and repeated in 12 to 24 hours if there be no improvement. McCullom uses in addition, red and yellow iodide of mercury locally, gr. $\frac{1}{2}$ to the ounce of vaseline, and atropine or cocaine as a mydriatic. Hermann Cohn, of Breslau recommended hourly pencillings of the palpebral conjunctiva with a 5 % solution of benzoate of soda, and declared that no patient, thus treated, lost an eye.

For diphtheria of other sites, such as the vulva, vagina, rectum, anus &c., and wounds, sulphur or any other local remedy, used for the throat, may be applied locally.

A FEW SELECTED CASES.
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Case 1. J. W., male, aged 10 years, was first seen December 14th, 1896. He had been ill for about 7 days. The whole throat was covered with diphtheritic membrane. The cervical glands were swollen. The child was very ill. Temperature, 100° Pulse 130.

Treatment. A mixture of Liquor Ferri Perchloridi and Chlorate of Potash was ordered to be given every hour, to be followed by insufflation of sublimed sulphur. The urine was found to be albuminous. As it was Saturday night, no anti-toxin could be obtained. On Monday, December 16th., antitoxin having been obtained, 500 units were injected. No effect was noticed. The child died on December 18th of toxæmia.

Judging from subsequent experience, 10,000 units of antitoxin might have saved the patient. It was ascertained that a sister of this patient had died a few years before of the same disease.

In the year 1905 the writer attended the mother and a brother of this patient for diphtheria. This seems to point to a family predisposition to the disease.

Case 2. J. Jones, male, aged 5 years was first seen December 21, 1895. He had been ill for 8 days. He was found to be suffering

from diphtheria of the throat. Treatment was similar to Case 1. The antitoxin had no noticeable effect. The patient died of assthenia 3 days later. The dose (500 units) of antitoxin was far too small. It is doubtful, even if an adequate dose had been injected, whether the patient would have recovered, seeing the late stage of the disease when it was administered.

At various times after this case there were 10 cases of diphtheria at the same house. The father, having learnt the symptoms of the disease always sought medical aid at the very beginning of the illness, so that treatment was begun within 24 hours of the commencement of the disease. All the cases, which were treated with sulphur insufflations and the iron mixture, recovered.

Case 3. J. H. J., male, aged 50 years, was

seen at the surgery, August 18th, 1896.

He had a patch of membrane about an inch in diameter on the posterior wall of the pharynx. He complained but little of his throat, his chief trouble being oedema of the feet and legs. The urine was found to be albuminous. Temperature -- normal. Treatment -- sulphur insufflations and the iron mixture. Recovery was speedy and uneventful.

Case 4. C. A. O., female, aged 29 years, was first seen September, 10th, 1897.

The tonsils were swollen, and covered with greyish membrane. Temperature 104° : Pulse, 135.

Treatment: sulphur insufflations and the iron mixture. The temperature came down to normal in 5 days, and the membrane cleared in 4 to 5 days. This case was complicated with nephritis, haematuria, and albuminuria. There were no paralytic sequelae. The writer attended this patient for the same disease on three subsequent occasions. The treatment was the same each time.

Case 5. J. M. male, aged 52 years. was first seen March 15th 1898. The tonsils

were much swollen, and covered with diphtheritic membrane. Treatment: the same as Case 4.

There was severe haemorrhage from the throat when the membrane was separating. The case was complicated with nephritis. There was also paralysis of the palate. This patient had diphtheria on three subsequent occasions.

Case 6. A. J. P. female, aged 30 years, was first seen August 22nd. 1898. She had

been ill with sore throat for two days. The throat was covered with diphtheritic membrane.

Temperature 102° : Treatment: the same as

Case 5. This treatment was effectual. On August 27th. the patient became much worse, the

temperature going up to 104° . Twenty four hours later a scarlet rash was found to cover the whole body. The throat also assumed a port wine redness, and the tongue became strawberry red. The same treatment was continued. The patient made a good recovery with no sequelae. The usual scarlet fever desquamation followed in due course.

Case 7. E. P. female, aged 5 years, a child of the previous patient was first seen April 9th. 1901. She was found to be suffering from diphtheria of the throat and nose. The nose was filled with yellowish grey membrane, and discharged a thin, foul, irritating fluid. There was intense foetor of the breath. Both tonsils were covered with greyish membrane. Treatment -- the same as the last cases with the addition of 500 units of antitoxin subcutaneously. She had severe epistaxis. She died of asthenia, due probably to toxæmia and loss of blood.

Case 8. A. J. E. male aged 2 years, was first seen May 1st. 1901. He had a patch of diphtheritic membrane on the hard palate. Treatment -- insufflations of sulphur and the iron mixture. This treatment caused an improvement in the symptoms, the membrane ceasing to spread. Owing to severe intestinal irritation

the sulphur had to be stopped. Thereupon the membrane began to spread again. A dose of 1,000 units diphtheria antitoxin was promptly injected, followed in 12 hours by a dose of 500 units. These two injections checked the spread of the membrane and effected a rapid cure. The membrane in this case seemed to disappear by a process of absorption.

Case 9. M. H. female, aged 6 years was first seen December 23th 1901. She had been ill for three days. When seen, she was very ill, having all the symptoms of laryngeal diphtheria. There was great prostration, and signs of laryngeal obstruction. Temperature: 101.4° Pulse, 135. Both tonsils were covered with diphtheritic membrane. It seemed to be a hopeless case of laryngeal diphtheria. Treatment -- insufflations of sulphur with the iron mixture. Hot linseed meal poultices, to be changed frequently, were ordered to be applied to the throat. Twelve hours later 4,000 units antitoxin were injected.

The next day the signs of laryngeal obstruction were less pronounced, the throat was better, and the patient's general aspect had improved. The following day the temperature was normal. She made a good recovery. This patient was undoubtedly saved by the antitoxin.

Case 10. N. E. female, aged 10 years, was first seen December 22nd. 1902. She had been ill a week. The throat was covered with diphtheritic membrane. Temperature -- 100 ; pulse, 120. Treatment -- insufflations of sulphur and the iron mixture, and an injection of 6,000 units antitoxin. She improved steadily and rapidly, the membrane disappearing from the throat in about 5 days. A fortnight after she was first seen, she was taken suddenly ill. She had great pain in the stomach and bowels, vomited frequently, and became rapidly cyanosed. She died, in 3 hours, of cardiac paralysis. Treatment of the cardiac crisis was of no avail.

Case 11. W. C. male, aged 5 years, was first seen April 22nd. 1905. His parents thought that he was suffering from mumps. There was extensive inflammation and membrane in the throat. There were also symptoms of extension to the larynx. The breath was very foul. There was great prostration. Treatment -- insufflations of sulphur. The iron mixture with the addition of strychnine was also prescribed. The following day, antitoxin having been then obtained, 5,000 units were injected. Two days later, although the membrane was separating, the child died of asthenia.

Case 12. J. G. aged 40 years, mother of the preceding patient, was first seen April 23rd. 1905. She had been in constant attendance on the last patient. The throat was extensively inflamed and covered with greyish membrane. Treatment -- insufflations of sulphur and the iron mixture. She made a good recovery. These two last cases show the importance of early treatment.

Case 13. H. M. W. female, aged $3\frac{1}{2}$ years, was first seen December 15th, 1903. Both tonsils were covered with diphtheritic membrane, and there was much glandular swelling. Temperature -- 103° ; Pulse 142. Treatment -- insufflations of sulphur and the iron mixture. For three days there was marked improvement. The patient then became worse, the temperature rising and symptoms of asthenia developing. A dose of 6,000 units ^{antitoxin} was thereupon administered. This was followed by rapid improvement in all the symptoms -- the temperature declining gradually. In five days again a similar relapse occurred. This again was checked by another injection of 6,000 units of antitoxin. There were two further relapses, occurring five days after the injections which were checked by 6,000 units of antitoxin as before. Altogether 24,000 units of antitoxin were injected -- the last injection not being

followed by a relapse. The child ultimately made a good recovery, with no paralytic sequelae.

Case 14. M. H. female, aged 30 years, was first seen October 9th 1906. Both tonsils were covered with diphtheritic membrane. She was not very ill. Treatment -- insufflations of sulphur and the iron mixture. She made a rapid recovery.

Case 15. M. E. H. female, aged 15 years, who had attended the last patient, was first seen October 12th, 1906. She had been ill for three days. The throat was swollen and red. Both* tonsils were covered with greyish membrane. Temperature -- 103° : Pulse 130. Treatment -- insufflations of sulphur and the iron mixture. She recovered slowly. In three weeks, right-sided paralysis developed, affecting chiefly the arm and leg. This was treated by electricity, the faradic current being used. Each application was followed by a decided improvement, both as regards sensation and muscular power.

Case 16. L. G. female, aged 6 years, was first seen October 16th 1906. She had been ill five days. The whole throat was blocked with dirty, yellowish grey membrane, which extended forwards into the mouth. The cervical glands were much swollen. There was albuminuria

Temperature -- 104.4° ; Pulse 135. There was intense foetor of the breath. The face was pale and the lips bluish. There were also signs of downward extension into the larynx.

Treatment -- insufflations of sulphur and the iron mixture were immediately prescribed.

Antitoxin having been obtained, 12,000 units were injected the next day. This seemed a hopeless case for any form of treatment except antitoxin. The following day there was decided improvement, the membrane beginning to get detached. No more antitoxin was found necessary. The child ultimately recovered, but was extremely weak for many weeks. There were no sequelae.

Case 17. G. J. male, aged 35 years, was first seen October 20th 1906. He had what seemed to be tonsillitis. Both tonsils were red and swollen, the left being the worse. No membrane was detected on any occasion. Several cases of diphtheria having occurred in the vicinity about this time, membrane was looked for every time the patient was seen. Treatment -- application of hot poultices and a mixture of iron and chlorate of potash.

The throat symptoms subsided gradually; but in a week or 10 days paralysis began to develop. The muscles of the palate were affected firstly, then the arms, and lastly the legs.

The patient became a complete cripple, being unable even to feed himself. The paralysis eventually passed in the same order as it occurred; palate, arms, legs. There was also sensory paralysis, preceded by formication and neuralgia. Unfortunately no bacteriological examination was made. Judging by the course of the disease one cannot help concluding that this was a case of catarrhal diphtheria. The paralysis was treated by electricity, the faradic current being employed. He was also given, iron, phosphorus, and strychnine. He ultimately recovered, but was unable to follow his employment for 6 months.

Case 18. G. B. male, aged 10 years, was first seen January 27th 1908, at 3 a.m.

Having had attacks of croup (laryngitis stridula) on several occasions he was supposed to be suffering from such an attack now. He had been ill two days. The tonsils were found to be enormously enlarged, blocking up the fauces. Both tonsils were covered with greyish membrane. The breath was extremely foul. Temperature 102° Pulse 140. The breathing was striderous. No albumen. Treatment -- insufflations of sulphur and the iron mixture were immediately prescribed. At 11 a.m. 8,000 units of antitoxin were injected. At 8 p.m., the respiratory distress was less marked. The temperature became normal the next

day and the patient made a slow uninterrupted recovery.

Case 19. E. C. male, aged 6 years, was first seen March 18th 1908. He had been ill 12 hours. He complained of sore throat and pain in the cervical glands. The fauces were red and both tonsils slightly swollen. On the right tonsil there was a small patch of greyish membrane about a $\frac{1}{2}$ inch in diameter. Temperature 100°. Pulse 120. Treatment -- insufflations of sulphur and the iron mixture.

At 11 a.m. the following day the temperature was 103.5°. The tonsils were now more swollen. The patch of membrane which had been observed on the right tonsil, could not now be seen; it seemed to have been enclosed in the swollen tonsil. At 3 p.m. 8, 000 units of antitoxin were injected. The following day the temperature was normal, and the tonsils were less swollen.

The patch of membrane which had been observed on the right tonsil, was again quite evident. There was now also a smaller patch of membrane on the left tonsil. The following day both tonsils were free from membrane. Except for an urticarial rash, which appeared on the sixth day after the injection of antitoxin, the recovery was rapid and uneventful.

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